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Stress-fiber mechanics and cell mechano-sensitivity

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ABSTRACT

In recent years, research in cell biology has shown that mechanics is a key to cell response, differentiation, and disease. For instance, an increasing number of observations have shown that the ability of cells to contract, spread, and differentiate is highly dependent on the stiffness and architecture of the surrounding matrix. Although the origins of these intriguing behaviors are still poorly understood, it is now clear that cells fully make use of cross-talks between mechanics, chemistry, and transport processes to organize their structure, generate forces, and make appropriate decisions.

To better understand the underlying mechanisms of mechano-transduction, this presentation will introduce a multiscale approach to the actin cytoskeleton of an adherent scale, spanning from the molecular to the cellular scale. At the cellular scale, the cytoskeleton is viewed as an active gel, which can acquire a specific structure and exert contractile forces in response to its mechanical environment. The way by which these forces arise and stabilize the cytoskeleton is explained in terms of a fine scale model of the interactions between the actin filaments and myosin motors found within each individual sarcomere of a stress fiber. At this scale, a cross-bridge model is used to explain the stabilization of active acto–myosin complex in the presence of so-called a catch-bond behavior between the two molecular units. The idea of a catch-bond response acto–myosin assembly was indeed discovered recently but never related to the mechano-sensitivity of stress-fibers. After further derivations, these concepts are summarized into a coupled system of differential equation whose solution is analyzed using numerical methods such as finite elements.

Numerical simulations show that the model is able to capture the dependency of cell contraction on substrate stiffness, adhesion or the application of external force on the cell boundary. The very good agreement between model predictions and experimental observations not only confirms that catch bonds may play a significant role in the mechano-sensitivity of adherent cells, but also pinpoint the importance of the hierarchical structure of stress-fibers across the scales.